

SEQUENCE LISTING

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<110> Shiroo, Masahiro
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<120> Regulation of Human Transient Receptor Potential Channel

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<150> PCT/EP03/03713

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<150> US 60/372,899

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Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
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Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
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Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
Page 22

Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
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His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val
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Val Ile Ser Val Thr Gly Gly Ala Lys Asn Phe Ala Leu Lys Pro Arg
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Met Arg Lys Ile Phe Ser Arg Leu Ile Tyr Ile Ala Gln Ser Lys Gly
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His Thr His Leu Leu Leu Val Asp Asn Gly Cys His Gly His Pro Thr
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Cys Ile Tyr Met Leu Ser Thr Asn Ile Leu Leu Val Asn Leu Leu Val
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Ala Met Phe Gly Tyr Thr Val Gly Thr Val Gln Glu Asn Asn Asp Gln
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980

985

990

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Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
Page 31

165

170

175

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 Gln His Phe Thr Ala Gln Pro Gly Val Gln Asn Phe Leu Ser Lys Gln
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 Trp Tyr Gly Glu Ile Ser Arg Asp Thr Lys Asn Trp Lys Ile Ile Leu
 675 680 685
 Cys Leu Phe Ile Ile Pro Leu Val Gly Cys Gly Phe Val Ser Phe Arg
 690 695 700
 Lys Lys Pro Val Asp Lys His Lys Lys Leu Leu Trp Tyr Tyr Val Ala
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Phe Phe Thr Ser Pro Phe Val Val Phe Ser Trp Asn Val Val Phe Tyr
725 730 735
Ile Ala Phe Leu Leu Leu Phe Ala Tyr Val Leu Leu Met Asp Phe His
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Ser Val Pro His Pro Pro Glu Leu Val Leu Tyr Ser Leu Val Phe Val
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Leu Phe Cys Asp Glu Val Arg Gln Trp Tyr Val Asn Gly Val Asn Tyr
770 775 780
Phe Thr Asp Leu Trp Asn Val Met Asp Thr Leu Gly Leu Phe Tyr Phe
785 790 795 800
Ile Ala Gly Ile Val Phe Arg Leu His Ser Ser Asn Lys Ser Ser Leu
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Tyr Ser Gly Arg Val Ile Phe Cys Leu Asp Tyr Ile Ile Phe Thr Leu
820 825 830
Arg Leu Ile His Ile Phe Thr Val Ser Arg Asn Leu Gly Pro Lys Ile
835 840 845
Ile Met Leu Gln Arg Met Leu Ile Asp Val Phe Phe Phe Leu Phe Leu
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Phe Ala Val Trp Met Val Ala Phe Gly Val Ala Arg Gln Gly Ile Leu
865 870 875 880
Arg Gln Asn Glu Gln Arg Trp Arg Trp Ile Phe Arg Ser Val Ile Tyr
885 890 895
Glu Pro Tyr Leu Ala Met Phe Gly Gln Val Pro Ser Asp Val Asp Gly
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Thr Thr Tyr Asp Phe Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys
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Pro Leu Cys Val Glu Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu
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Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile
945 950 955 960
Leu Leu Val Asn Leu Leu Val Ala Met Phe Gly Tyr Thr Val Gly Thr
965 970 975
Val Gln Glu Asn Asn Asp Gln Val Trp Lys Phe Gln Arg Tyr Phe Leu
980 985 990

Val Gln Glu Tyr Cys Ser Arg Leu Asn Ile Pro Phe Pro Phe Ile Val
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Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys
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Cys Lys Glu Lys Asn Met Glu Ser Ser Val Cys Cys Phe Lys Asn
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Glu Asp Asn Glu Thr Leu Ala Trp Glu Gly Val Met Lys Glu Asn
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Tyr Leu Val Lys Ile Asn Thr Lys Ala Asn Asp Thr Ser Glu Glu
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Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala
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Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
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Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp
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Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
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Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
115 120 125

His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
130 135 140

Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile
145 150 155 160

Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
165 170 175

Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
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Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp
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Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu
210 215 220

Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro
225 230 235 240

Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn
245 250 255

Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu
260 265 270

Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly
275 280 285

Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu
290 295 300

Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val
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Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val
325 330 335

Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe
340 345 350

Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp.
355 360 365

Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
370 375 380

Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
Page 36

385

390

395

400

Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
 405 410 415

Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
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Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
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Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
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Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
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Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
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Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu
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Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu
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Gln His Phe Ile Ala Gln Pro Gly Val Gln Asn Phe Leu Ser Lys Gln
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Trp Tyr Gly Glu Ile Ser Arg Asp Thr Lys Asn Trp Lys Ile Ile Leu
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 755 760 765
 Leu Phe Cys Asp Glu Val Arg Gln Trp Tyr Val Asn Gly Val Asn Tyr
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 Phe Thr Asp Leu Trp Asn Val Met Asp Thr Leu Gly Leu Phe Tyr Phe
 785 790 795 800
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 Tyr Ser Gly Arg Val Ile Phe Cys Leu Asp Tyr Ile Ile Phe Thr Leu
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 Arg Gln Asn Glu Gln Arg Trp Arg Trp Ile Phe Arg Ser Val Ile Tyr
 885 890 895
 Glu Pro Tyr Leu Ala Met Phe Gly Gln Val Pro Ser Asp Val Asp Gly
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 Thr Thr Tyr Asp Phe Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys
 915 920 925
 Pro Leu Cys Val Glu Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu
 930 935 940

Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile
945 950 955 960

Leu Leu Val Asn Leu Leu Val Ala Met Phe Gly Tyr Thr Val Gly Thr
965 970 975

Val Gln Glu Asn Asn Asp Gln Val Trp Lys Phe Gln Arg Tyr Phe Leu
980 985 990

Val Gln Glu Tyr Cys Ser Arg Leu Asn Ile Pro Phe Pro Phe Ile Val
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Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys
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Cys Lys Glu Lys Asn Met Glu Ser Ser Val Cys Cys Phe Lys Asn
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Glu Asp Asn Glu Thr Leu Ala Trp Glu Gly Val Met Lys Glu Asn
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Tyr Leu Val Lys Ile Asn Thr Lys Ala Asn Asp Thr Ser Glu Glu
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Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala
50 55 60

Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
65 70 75 80

Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp
Page 39

85

90

95

Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
100 105 110

Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
115 120 125

His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
130 135 140

Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile
145 150 155 160

Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
165 170 175

Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
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Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp
195 200 205

Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu
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Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro
225 230 235 240

Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn
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Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu
260 265 270

Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly
275 280 285

Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu
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Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val
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Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val
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Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe
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Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp
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Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
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 Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
 385 390 395 400
 Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
 405 410 415
 Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
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 Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
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 Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
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 Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
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 His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val
 485 490 495
 Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
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 Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys
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 Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val
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 Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile
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 Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu
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 Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu
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 Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr
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Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala
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Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
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Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp
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Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
100 105 110

Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
115 120 125

His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
130 135 140

Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile
145 150 155 160

Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
165 170 175

Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
180 185 190

Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp
195 200 205

Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu
 210 215 220
 Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro
 225 230 235 240
 Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn
 245 250 255
 Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu
 260 265 270
 Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly
 275 280 285
 Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu
 290 295 300
 Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val
 305 310 315 320
 Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val
 325 330 335
 Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe
 340 345 350
 Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp
 355 360 365
 Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
 370 375 380
 Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
 385 390 395 400
 Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
 405 410 415
 Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
 420 425 430
 Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
 435 440 445
 Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
 450 455 460
 Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
 465 470 475 480

His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val
485 490 495

Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
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Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys
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Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val
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Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile
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Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg
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Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu
580 585 590

Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu
595 600 605

Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr
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Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu
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Ala Trp Gly Gly Ser Asn Cys Leu Glu Leu Ala Val Glu Ala Thr Asp
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Gln His Phe Ile Ala Gln Pro Gly Val Gln Asn Phe Leu Ser Lys Gln
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Trp Tyr Gly Glu Ile Ser Arg Asp Thr Lys Asn Trp Lys Ile Ile Leu
675 680 685

Cys Leu Phe Ile Ile Pro Leu Val Gly Cys Gly Phe Val Ser Phe Arg
690 695 700

Lys Lys Pro Val Asp Lys His Lys Lys Leu Leu Trp Tyr Tyr Val Ala
705 710 715 720

Phe Phe Thr Ser Pro Phe Val Val Phe Ser Trp Asn Val Val Phe Tyr
725 730 735

Ile Ala Phe Leu Leu Leu Phe Ala Tyr Val Leu Leu Met Asp Phe His
740 745 750

Ser Val Pro His Pro Pro Glu Leu Val Leu Tyr Ser Leu Val Phe Val
Page 44

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Arg	Leu	Ile	His	Ile	Phe	Thr	Val	Ser	Arg	Asn	Leu	Gly	Pro	Lys	Ile
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Ile	Met	Leu	Gln	Arg	Met	Leu	Ile	Asp	Val	Phe	Phe	Phe	Leu	Phe	Leu
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Glu	Pro	Tyr	Leu	Ala	Met	Phe	Gly	Gln	Val	Pro	Ser	Asp	Val	Asp	Gly
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Thr	Thr	Tyr	Asp	Phe	Ala	His	Cys	Thr	Phe	Thr	Gly	Asn	Glu	Ser	Lys
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Pro	Leu	Cys	Val	Glu	Leu	Asp	Glu	His	Asn	Leu	Pro	Arg	Phe	Pro	Glu
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Trp	Ile	Thr	Ile	Pro	Leu	Val	Cys	Ile	Tyr	Met	Leu	Ser	Thr	Asn	Ile
945					950					955					960
Leu	Leu	Val	Asn	Leu	Leu	Val	Ala	Met	Phe	Gly	Tyr	Thr	Val	Gly	Thr
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Val	Gln	Glu	Asn	Asn	Asp	Gln	Val	Trp	Lys	Phe	Gln	Arg	Tyr	Phe	Leu
			980					985					990		
Val	Gln	Glu	Tyr	Cys	Ser	Arg	Leu	Asn	Ile	Pro	Phe	Pro	Phe	Ile	Val
		995					1000					1005			
Phe	Ala	Tyr	Phe	Tyr	Met	Val	Val	Lys	Lys	Cys	Phe	Lys	Cys	Cys	
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Cys	Lys	Glu	Lys	Asn	Met	Glu	Ser	Ser	Val	Cys	Cys	Phe	Lys	Asn	
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Tyr Leu Val Lys Ile Asn Thr Lys Ala Asn Asp Thr Ser Glu Glu
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Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
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Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp
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Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
100 105 110

Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
115 120 125

His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
130 135 140

Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile
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Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
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Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
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Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro
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Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn
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Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu
260 265 270

Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly
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Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu
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Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val
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Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val
325 330 335

Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe
340 345 350

Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp
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Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
370 375 380

Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
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Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
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Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
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Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
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Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
Page 47

450 455 460
 Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
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 His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val
 485 490 495
 Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
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 Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys
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 Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val
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 Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile
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 Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu
 580 585 590
 Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu
 595 600 605
 Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr
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 35 40 45

Phe Lys Lys Arg Glu Cys Val Phe Phe Thr Lys Asp Ser Lys Ala Thr
 50 55 60
 Glu Asn Val Cys Lys Cys Gly Tyr Ala Gln Ser Gln His Met Glu Gly
 65 70 75 80
 Thr Gln Ile Asn Gln Ser Glu Lys Trp Asn Tyr Lys Lys His Thr Lys
 85 90 95
 Glu Phe Pro Thr Asp Ala Phe Gly Asp Ile Gln Phe Glu Thr Leu Gly
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 Lys Lys Gly Lys Tyr Ile Arg Leu Ser Cys Asp Thr Asp Ala Glu Ile
 115 120 125
 Leu Tyr Glu Leu Leu Thr Gln His Trp His Leu Lys Thr Pro Asn Leu
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 Val Ile Ser Val Thr Gly Gly Ala Lys Asn Phe Ala Leu Lys Pro Arg
 145 150 155 160
 Met Arg Lys Ile Phe Ser Arg Leu Ile Tyr Ile Ala Gln Ser Lys Gly
 165 170 175
 Ala Trp Ile Leu Thr Gly Gly Thr His Tyr Gly Leu Met Lys Tyr Ile
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 Gly Glu Val Val Arg Asp Asn Thr Ile Ser Arg Ser Ser Glu Glu Asn
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 Ile Val Ala Ile Gly Ile Ala Ala Trp Gly Met Val Ser Asn Arg Asp
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 Thr Leu Ile Arg Asn Cys Asp Ala Glu Gly Tyr Phe Leu Ala Gln Tyr
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 Leu Met Asp Asp Phe Thr Arg Asp Pro Leu Cys Ile Leu Asp Asn Asn
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 His Thr His Leu Leu Val Asp Asn Gly Cys His Gly His Pro Thr
 260 265 270
 Val Glu Ala Lys Leu Arg Asn Gln Leu Glu Lys Tyr Ile Ser Glu Arg
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 Thr Ile Gln Asp Ser Asn Tyr Gly Gly Lys Ile Pro Ile Val Cys Phe
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 Ala Gln Gly Gly Gly Lys Glu Thr Leu Lys Ala Ile Asn Thr Ser Ile
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Lys Asn Lys Ile Pro Cys Val Val Val Glu Gly Ser Gly Gln Ile Ala
325 330 335

Asp Val Ile Ala Ser Leu Val Glu Val Glu Asp Ala Leu Thr Ser Ser
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Ala Val Lys Glu Lys Leu Val Arg Phe Leu Pro Arg Thr Val Ser Arg
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Leu Pro Glu Glu Glu Thr Glu Ser Trp Ile Lys Trp Leu Lys Glu Ile
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Leu Leu Glu Trp Asn Gln Leu Asp Leu Ala Asn Asp Glu Ile Phe Thr
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Gly Leu Asn Leu Arg Lys Phe Leu Thr His Asp Val Leu Thr Glu Leu
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Phe Ser Asn His Phe Ser Thr Leu Val Tyr Arg Asn Leu Gln Ile Ala
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Lys Asn Ser Tyr Asn Asp Ala Leu Leu Thr Phe Val Trp Lys Leu Val
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Ala Asn Phe Arg Arg Gly Phe Arg Lys Glu Asp Arg Asn Gly Arg Asp
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Glu Met Asp Ile Glu Leu His Asp Val Ser Pro Ile Thr Arg His Pro
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Leu Gln Ala Leu Phe Ile Trp Ala Ile Leu Gln Asn Lys Lys Glu Leu
565 570 575

Ser Lys Val Ile Trp Glu Gln Thr Arg Gly Cys Thr Leu Ala Ala Leu
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Gly Ala Ser Lys Leu Leu Lys Thr Leu Ala Lys Val Lys Asn Asp Ile
Page 50

595					600					605					
Asn	Ala	Ala	Gly	Glu	Ser	Glu	Glu	Leu	Ala	Asn	Glu	Tyr	Glu	Thr	Arg
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Ala	Tyr	Val	Leu	Leu	Met	Asp	Phe	His	Ser	Val	Pro	His	Pro	Pro	Glu
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Gln	Trp	Tyr	Val	Asn	Gly	Val	Asn	Tyr	Phe	Thr	Asp	Leu	Trp	Asn	Val
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Met	Asp	Thr	Leu	Gly	Leu	Phe	Tyr	Phe	Ile	Ala	Gly	Ile	Val	Phe	Arg
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Leu	His	Ser	Ser	Asn	Lys	Ser	Ser	Leu	Tyr	Ser	Gly	Arg	Val	Ile	Phe
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Cys	Leu	Asp	Tyr	Ile	Ile	Phe	Thr	Leu	Arg	Leu	Ile	His	Ile	Phe	Thr
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Val	Ser	Arg	Asn	Leu	Gly	Pro	Lys	Ile	Ile	Met	Leu	Gln	Arg	Met	Leu
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Ile	Asp	Val	Phe	Phe	Phe	Leu	Phe	Leu	Phe	Ala	Val	Trp	Met	Val	Ala
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Gly Gln Val Pro Ser Asp Val Asp Gly Thr Thr Tyr Asp Phe Ala His
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Cys Thr Phe Thr Gly Asn Glu Ser Lys Pro Leu Cys Val Glu Leu Asp
930 935 940

Glu His Asn Leu Pro Arg Phe Pro Glu Trp Ile Thr Ile Pro Leu Val
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Cys Ile Tyr Met Leu Ser Thr Asn Ile Leu Leu Val Asn Leu Leu Val
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Arg Ser Thr Asp Leu Ser Tyr Ser Glu Ser Ala Ser Phe Tyr Ala Ala
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Phe Arg Thr Gln Thr Cys Pro Ile Met Ala Ser Trp Asp Leu Val Asn
65 70 75 80

Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe Thr Lys
85 90 95

Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala Gln Ser
100 105 110

Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp Asn Tyr
115 120 125

Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp Ile Gln
130 135 140

Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser Cys Asp
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Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp His Leu
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Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys Asn Phe
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Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile Tyr Ile
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Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His Tyr Gly
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Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile Ser Arg
225 230 235 240

Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp Gly Met
245 250 255

Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu Gly Tyr
260 265 270

Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro Leu Tyr
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275

280

285

Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn Gly Cys
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His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu Glu Lys
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Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly Lys Ile
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Pro Ile Val Cys Phe Ala Gln Gly Gly Lys Glu Thr Leu Lys Ala
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Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val Glu Asp
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Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp Ile Lys
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Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val Ile Lys
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Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser Tyr Ala
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Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn Trp Asn
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Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu Ala Asn
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Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Lys Ser Lys Pro Arg
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 Ala Ala Gly Glu Ser Glu Glu Leu Ala Asn Glu Tyr Glu Thr Arg Ala
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 Cys Gly Thr Asp Ile Ala Ser Gly Thr His Arg Pro Asp Gly Gly Glu
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Trp Asn Val Val Phe Tyr Ile Ala Phe Leu Leu Leu Phe Ala Tyr Val
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Leu Leu Met Asp Phe His Ser Val Pro His Pro Pro Glu Leu Val Leu
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Tyr Ser Leu Val Phe Val Leu Phe Cys Asp Glu Lys Arg Lys Thr Ala
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Met Asp Gln Thr Asp Glu Asp Leu Phe Pro Tyr Gly Ala Phe Tyr Gln
900 905 910

Phe Leu Met Ile Ser Arg Ser Phe Arg Gly Glu Glu Met Ser Ile Gly
915 920 925

Lys Gln His
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